

WHAT IS CLAIMED IS :

1. A protein possessing a specific urate oxidase activity of at least 16 U/mg and having the following sequence: (SEQUENCE ID NO. 1)

Ser Ala Val Lys Ala Ala Arg Tyr Gly Lys Asp Asn Val Arg Val Tyr Lys
Val His Lys Asp Glu Lys Thr Gly Val Gln Thr Val Tyr Glu Met Thr Val
Cys Val Leu Leu Glu Gly Glu Ile Glu Thr Ser Tyr Thr Lys Ala Asp Asn
Ser Val Ile Val Ala Thr Asp Ser Ile Lys Asn Thr Ile Tyr Ile Thr Ala
Lys Gln Asn Pro Val Thr Pro Pro Glu Leu Phe Gly Ser Ile Leu Gly Thr
His Phe Ile Glu Lys Tyr Asn His Ile His Ala Ala His Val Asn Ile Val
Cys His Arg Trp Thr Arg Met Asp Ile Asp Gly Lys Pro His Pro His Ser
Phe Ile Arg Asp Ser Glu Glu Lys Arg Asn Val Gln Val Asp Val Val Glu
Gly Lys Gly Ile Asp Ile Lys Ser Ser Leu Ser Gly Leu Thr Val Leu Lys
Ser Thr Asn Ser Gln Phe Trp Gly Phe Leu Arg Asp Glu Tyr Thr Thr Leu
Lys Glu Thr Trp Asp Arg Ile Leu Ser Thr Asp Val Asp Ala Thr Trp Gln
Trp Lys Asn Phe Ser Gly Leu Gln Glu Val Arg Ser His Val Pro Lys Phe
Asp Ala Thr Trp Ala Thr Ala Arg Glu Val Thr Leu Lys Thr Phe Ala Glu
Asp Asn Ser Ala Ser Val Gln Ala Thr Met Tyr Lys Met Ala Glu Gln Ile
Leu Ala Arg Gln Gln Leu Ile Glu Thr Val Glu Tyr Ser Leu Pro Asn Lys
His Tyr Phe Glu Ile Asp Leu Ser Trp His Lys Gly Leu Gln Asn Thr Gly
Lys Asn Ala Glu Val Phe Ala Pro Gln Ser Asp Pro Asn Gly Leu Ile Lys
Cys Thr Val Gly Arg Ser Ser Leu Lys Ser Lys Leu

preceded if appropriate, by a methionine, or having a substantial degree of homology with that sequence.

2. A protein according to claim 1, possessing a specific urate oxidase activity of at least 30 U/mg.

3. A protein according to claim 1 or 2, which presents, by analysis on a bidimensional gel, a spot of molecular mass of about 33.5 kDa and an isoelectric point around 8.0, representing at least 90 % of the protein mass.

4. A protein according to anyone of claims 1 to 3, having a purity degree, determined by liquid chromatography on a C8 grafted silica column, higher than 80 %.

5. A protein according to anyone of claims 1 to 4, having an isoelectric point around 8.0.

6. A protein according to anyone of claims 1 to 4, which carries a blocking group on the amino-terminal serine having preferably a molecular mass around 43 units of atomic mass.

7. A drug containing a protein according to anyone of claims 1 to 6.

8. A recombinant gene which has the DNA sequence coding for the protein having the following sequence: (SEQUENCE ID NO. 2)

Met Ser Ala Val Lys Ala Ala Arg Tyr Gly Lys Asp Asn Val Arg Val
Tyr Lys Val His Lys Asp Glu Lys Thr Gly Val Gln Thr Val Tyr Glu
Met Thr Val Cys Val Leu Leu Glu Gly Glu Ile Glu Thr Ser Tyr Thr Lys
Ala Asp Asn Ser Val Ile Val Ala Thr Asp Ser Ile Lys Asn Thr Ile Tyr
Ile Thr Ala Lys Gln Asn Pro Val Thr Pro Pro Glu Leu Phe Gly Ser Ile
Leu Gly Thr His Phe Ile Glu Lys Tyr Asn His Ile His Ala Ala His Val
Asn Ile Val Cys His Arg Trp Thr Arg Met Asp Ile Asp Gly Lys Pro
His Pro His Ser Phe Ile Arg Asp Ser Glu Glu Lys Arg Asn Val Gln
Val Asp Val Val Glu Gly Lys Gly Ile Asp Ile Lys Ser Ser Leu Ser Gly
Leu Thr Val Leu Lys Ser Thr Asn Ser Gln Phe Trp Gly Phe Leu Arg Asp
Glu Tyr Thr Thr Leu Lys Glu Thr Trp Asp Arg Ile Leu Ser Thr Asp Val
Asp Ala Thr Trp Gln Trp Lys Asn Phe Ser Gly Leu Gln Glu Val Arg Ser
His Val Pro Lys Phe Asp Ala Thr Trp Ala Thr Ala Arg Glu Val Thr Leu
Lys Thr Phe Ala Glu Asp Asn Ser Ala Ser Val Gln Ala Thr Met Tyr Lys
Met Ala Glu Gln Ile Leu Ala Arg Gln Gln Leu Ile Glu Thr Val Glu Tyr
Ser Leu Pro Asn Lys His Tyr Phe Glu Ile Asp Leu Ser Trp His Lys Gly
Leu Gln Asn Thr Gly Lys Asn Ala Glu Val Phe Ala Pro Gln Ser Asp Pro
Asn Gly Leu Ile Lys Cys Thr Val Gly Arg Ser Ser Leu Lys Ser Lys Leu

9. A recombinant gene according to claim 8, which permits the expression in the prokaryotic microorganisms.

10. A recombinant gene according to claim 9, wherein the DNA sequence contains the followings sequence (SEQUENCE ID NO. 3):

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ATGTCTGCGG TAAAAGCAGC GCGCTACGGC AAGGACAATG TTCGCGTCTA
CAAGGTTTAC AAGGACGAGA AGACCGGTGT CCAGACGGTG TACGAGATGA
CCGTCTGTGT GCTTCTGGAG GGTGAGATTG AGACCTCTTA CACCAAGGCC
GACAACAGCG TCATTGTGCG AACCGACTCC ATTAAGAACA CCATTTACAT
CACCGCCAAG CAAACCCCG TTAATCCTCC CGAGCTGTTC GGCTCCATCC
TGGGCACACA CTTCAATTGAG AAGTACAACC ACATCCATGC CGCTCACGTC
AACATTGTCT GCCACCGCTG GACCCGGATG GACATTGACG GCAAGCCACA
CCCTCACTCC TTCATCCGCG ACAGCGAGGA GAAGCGGAAT GTGCAGGTGG
ACGTGGTCTGA GGGCAAGGGC ATCGATATCA AGTCGTCTCT GTCCGGCCTG
ACCGTGCTGA AGAGCACCAA CTCGAGTTT TGGGCTTCC TCGTGACGA
GTACACCACA CTTAAGGAGA CCTGGGACCG TATCCTGAGC ACCGACGTCG
ATGCCACTTG GCAGTGGGAG AATTTCACTG GACTCCAGGA GGTCCGCTCG
CACGTGCCTA AGTTCGATGC TACCTGGGCG ACTGCTCGCG AGGTCACTCT
GAAGACTTTT GCTGAAGATA ACAGTCCAG CGTGCAGGCC ACTATGTACA
AGATGGCAGA GCAAATCCTG GCGCGCCAGC AGCTGATCGA GACTGTGCGAG
TACTCGTTGC CTAACAAGCA CTATTTGAA ATCGACTGA GCTGGCACAA
GGGCCTCCAA AACACCGGCA AGAACGCCGA GGTCTTCGCT CCTCAGTCGG
ACCCCAACGG TCTGATCAAG TGTACCGTCG GCCGGTCCTC TCTGAAGTCT
AAATTG.

11. A recombinant gene according to claim 8, which permits the expression in the eukaryotic cells.

12. A recombinant gene according to claim 11, wherein the DNA sequence contains the following sequence:

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SEQUENCE ID NO. 4

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ATGTCTGCTG TTAAGGCTGC TAGATACGGT AAGGACAACG TTAGACTCTA
CAAGGTTTAC AAGGACGAGA AGACCGGTGT CCAGACGGTG TACGAGATGA
CCGTCTGTGT GCTTCTGGAG GGTGAGATTG AGACCTCTTA CACCAAGGCC
GACAACAGCG TCATTGTCGC AACCGACTCC ATTAAGAACA CCATTTACAT
CACCGCCAAG CAGAACCCCG TTAATCCTCC CGAGCTGTTT GGCTCCATCC
TGGGCACACA CTTCATTGAG AAGTACAACC ACATCCATGC CGCTCACGTC
AACATTGTCT GCCACCGCTG GACCCGGATG GACATTGACG GCAAGCCACA
CCCTCACTCC TTCATCCGCG ACAGCGAGGA GAAGCGGAAT GTGCAGGTGG
ACGTGGTCGA GGGCAAGGGC ATCGATATCA AGTCGTCTCT GTCCGGCCTG
ACCGTGCTGA AGAGCACCAA CTCGCAGTTC TGGGGCTTCC TGCCTGACGA
GTACACCACA CTTAAGGAGA CCTGGGACCG TATCCTGAGC ACCGACGTCG
ATGCCACTTG GCAGTGGAAG AATTCAGTG GACTCCAGGA GGTCCGCTCG
CACGTGCCTA AGTTCGATGC TACCTGGGCC ACTGCTCGCG AGGTCACTCT
GAAGACTTTT GCTGAAGATA ACAGTGCCAG CGTGCAGGCC ACTATGTACA
AGATGGCAGA GCAAATCCTG GCGCGCCAGC AGCTGATCGA GACTGTGCGAG
TACTCGTTGC CTAACAAGCA CTATTTTCGAA ATCGACCTGA GCTGGCACAA
GGGCCTCCAA AACACCGGCA AGAACGCCGA GGTCTTCGCT CCTCAGTCGG
ACCCCAACGG TCTGATCAAG TGTACCGTCG GCCGGTCCTC TCTGAAGTCT
AAATTG.

13. A recombinant gene according to claim 8, which permits the expression in the animal cells.

14. A recombinant gene according to claim 13, wherein the DNA sequence contains the following sequence:

(SEQUENCE ID NO. 6)

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-ATGTC CGCAGTAAAA GCAGCCCGCT ACGGCAAGGA
CAATGTCCGC GTCTACAAGG TTCACAAGGA CGAGAAGACC GGTGTCCAGA
CGGTGTACGA GATGACCGTC TGTGTGCTTC TGGAGGGTGA GATTGAGACC
TCTTACACCA AGGCCGACAA CAGCGTCATT GTCGCAACCG ACTCCATTAA
GAACACCATT TACATCACCG CCAAGCAGAA CCCCGTTACT CCTCCCAGC
TGTTCCGGCTC CATCCTGGGC ACACACTTCA TTGAGAAGTA CAACCACATC
CATGCCGCTC ACGTCAACAT TGTCTGCCAC CGCTGGACCC GGATGGACAT
TGACGGCAAG CCACACCCTC ACTCCTTCAT CCGCGACAGC GAGGAGAAGC
GGAATGTGCA GGTGGACGTG GTCGAGGGCA AGGGCATCGA TATCAAGTCG
10 TCTCTGTCCG GCCTGACCGT GCTGAAGAGC ACCAACTCGC AGTTCTGGGG
CTTCTGCGT GACGAGTACA CCACACTTAA GGAGACCTGG GACCGTATCC
TGAGCACCGA CGTCGATGCC ACTGGCGGT GGAAGAATTT CAGTGGACTC
CAGGAGGTCC GCTCGCACGT GCCTAAGTTC GATGCTACCT GGGCCACTGC
TCGCGAGGTC ACTCTGAAGA CTTTGCTGA AGATAACAGT GCCAGCGTGC
15 AGGCCACTAT GTACAAGATG SCAGAGCAAA TCCTGGCGCG CCAGCAGCTG
ATCGAGACTG TCGAGTACTC GTTGCTAAC AAGCACTATT TCGAAATCGA
CCTGAGCTGG CACAAGGGCC TCCAAAACAC CGGCAAGAAC GCCGAGGTCT
TCGCTCCTCA GTCGGACCCC AACGGTCTGA TCAAGTGATC CGTCGGCCGG
TCCTCTCTGA AGTCTAAATT G

20 preceded by a non-translated 5' sequence favoring expression in animal cells,

15. Recombinant gene according to claim 14, wherein the non-translated 5' sequence favoring expression in animal cells comprises the sequence AGCTTGCCGCCACT, located immediately upstream from the sequence described in claim 14.

25 16. An expression vector carrying a recombinant gene according to any one of claims 8 to 15 with the means necessary for its expression.

17. An expression vector according to claim 16, which carries at least one selection marker.

30 18. An expression vector according to claim 17, which has the characteristics of one of plasmids pEMR469, pEMR473, and pEMR 515.

19. Prokaryotic microorganisms which are transformed by an expression vector according to claim 16, carrying a recombinant gene according to claim 9.

20. Eukaryotic cells which are transformed by one of the expression vectors according to any one of claims 16 to 18, carrying the recombinant gene according to claim 11.
- 05 21. A strain of Saccharomyces cerevisiae which is transformed by one of the expression vectors according to any one of claims 16 to 18.
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22. A strain according to claim 21, which carries a mutation on at least one of the genes responsible for the synthesis of leucine or uracil.
- 10 23. A strain according to claim 22, which carries a mutation on at least one of the LEU2 and URA3 genes.
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24. A process for producing a recombinant urate oxidase which comprises the steps of :
- 15 1) cultivating a strain according to claims 21 to 23 ;
- 2) lysing the cells ;
- 3) isolating and purifying the recombinant urate oxidase contained in the lysate.
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25. Animal cells containing a recombinant gene according to claim 13 with the means necessary for its expression.
- 20 26. Animal cells containing an expression vector according to claim 16, carrying a recombinant gene according to claim 14.
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